

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/IB2004/001728

International filing date (day/month/year)
26.05.2004

Priority date (day/month/year)
29.05.2003

International Patent Classification (IPC) or both national classification and IPC
C07H17/08, A61K31/7048

Applicant
QUIMICA SINTETICA, S.A.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/IB2004/001728

Box No. II Priority

1. ☒ The following document has not been furnished:

- ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).
- ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	11-23
	No: Claims	1-10,24-27
Inventive step (IS)	Yes: Claims	---
	No: Claims	1-27
Industrial applicability (IA)	Yes: Claims	1-27
	No: Claims	---

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: WO 02/07736 A (CADILA PHARMACEUTICALS LTD ; KHAMAR BAKULESH MAFATLAL (IN)) 31 January 2002 (2002-01-31)
- D2: EP-A-1 075 837 (S I F I SOCIETA IND FARMACEUTI) 14 February 2001 (2001-02-14)
- D3: EP-A-0 307 128 (PFIZER) 15 March 1989 (1989-03-15)

Claims 1-10, 24-27 :

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-10, 24-27 is not new in the sense of Article 33(2) PCT.

The document D1 discloses a liquid pharmaceutical composition consisting of Azithromycin, citric acid (and Sodium hydroxide) thereby disclosing a citrate salt of azithromycin in solution.

D2 discloses azithromycin formulation for ophthalmic uses consisting in mixing azithromycin to citric acid (in the presence of phosphate) (see paragraph 13) thereby disclosing a citrate salt of azithromycin in solution.

As the subject-matter of claims 1-10, 24,25 does not specify if the salt of azithromycin/citric acid is in solution or in the solid state, the subject-matter these claims is anticipated by D1 and D2

D3 discloses the use azithromycin citric acid salt (see ex. 5) as an anti-protozoal agent. As it is well known that azithromycin (salts or not, the active ingredient being anyway azithromycin) are useful as antibacterial agents as well as antiprotozoal agents (see D3), the subject-matter of claim claims 26-27 is not considered new.

Claim 11 :

Since none of the available prior art discloses the azithromycin citric acid salt in a solid amorphous state, the subject-matter of claim 11 is considered new.

Nevertheless, as D1-D2 discloses the fact that azithromycin citric acid salt in solution between certain pH ranges stabilizes the formulation, as solid form of this salt is also expected to be more stable, the two nitrogen atoms being "better protected" against oxidation.

Therefore, the subject-matter of claim 11 is not considered inventive contrary to Art. 33(3) PCT.

Claims 12-23 :

The subject-matter of claims 12-23 is considered new in the light of the available prior art.

Nevertheless, the process of claims 12-23, which basically consist in dissolving/mixing two components (an acid and a base) and eventually isolating the salt thus formed afterwards, is so simple that it is considered trivial, and achievable by any man skilled in the art with ordinary basic knowledge of organic chemistry.

Thus claims 12-23 are not considered inventive contrary to Art. 33(3) PCT.

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